REMARKS

In response to the above Office Action, claims 32, 37, 39, and 41 have been amended to more particularly claim applicants' invention.

More specifically, main claim 32 now recites in the preamble that the cilostazol preparation is for "oral administration" and that the preparation in the form of powder, or granule or pill, or table or a capsule is for "orally administering the preparation to a human." Support for this can be found on page 21, line 19 and in Test Example 10 on page 68.

Main claim 32 was also amended to limit the average particle diameter of the fine powder of cilostazol to "from 2 to 10 μm." Support for the upper limit can be found in former claim 32. Support for the lower limit can be found in Examples 8 to 28 on pages 33-45. Claims 37, 39, and 41 have been amended to be consistent with amended claim 32.

Finally, new claims 49 and 50 have been added to more particularly claim the invention. Support for the claims can be found in claim 32.

It is not believed the amendments to the claims or the new claims introduce any new matter and their entry is therefore requested.

In the Office Action, the Examiner rejected claims 32-45 and 48 under 35 U.S.C. §103(a) for being obvious over WO 97/48382 (hereafter WO'382) in view of U.S. Patent No. 5,145,684 to Liversidge et al. (hereafter Liversidge). The indicated allowance of the subject matter of claims 46 and 47 is appreciated. However, in view of the amendment to claim 32 it is believed claims 32-45 and 48 also now contain allowable subject matter. Reconsideration of the rejection and allowance of all of the claims is therefore requested.

WO'382 was first cited by Examiner Jagoe in the Office Action of October 28, 2002 as a primary reference and again in the Office Action of August 1, 2003 as a secondary reference. As pointed out in the Replies to these Office Actions and as acknowledged by the Examiner in this Office Action, WO'382 may teach the combination of cilostazol and a sustained release material, but, significantly, it fails to teach the claimed particle size of the cilostazol as it was defined then, i.e., 10 μm or less, or as it is defined now "from 2 to 10 μm."

This is an important feature of applicants' invention as demonstrated by the Rule 132 Declaration filed April 28, 2003. Perhaps the current Examiner is not aware of this Declaration, and if so, it would be appreciated if he would consider its contents in the future prosecution of this case. Specifically the Declaration concluded that tablets prepared by using cilostazol within the claimed particle size (i.e., of from 2.0 to 5.4 μm) had much higher dissolution rates than that of tablets prepared by using cilostazol having a higher average particle size, i.e., 22.2 μm.

Liversidge, cited by the Examiner and discussed on page 3 of the specification, discloses particles consisting essentially of a crystalline drug substance having a surface modifier absorbed on the surface in an amount sufficient to maintain an effective average particle size of less than about 400 nm wherein the bioavailability is increased. See also claims 1 and 16, etc. of Liversidge.

However, as applicants point out on page 4, lines 12 to 18 of the specification, the present inventors invented a preparation capable of remarkably increasing absorption of cilostazol in the lower portion of the digestive tract, by incorporating a

dispersing and/or solubilizing agent to a fine powder of cilostazol . . . without adjusting the powder to average particle size of less than about 400 nm.

In Liversidge it is essential that the effective average particle size of the drug substance be less than about 400 nm. It can be prepared from a coarse drug substance selected of less than about 100 μm as determined by sieve analysis (see column 2, lines 38-43 and 47-55 as well as column 5, lines 41 to 61) via a process for micronization as described in claims 16 and 17 of Liversidge. Nothing is taught about a particle size for the final crystalline drug substance of higher than 400 nm (0.4 μm).

Accordingly, since neither WO'382 nor Liversidge teach the claimed particle range of "from 2 to 10 μm" of claim 32 or the more limited ranges of "from 2 to 7" μm or from "2 to 5 μm" of claims 37, 39, and 41, it is submitted the claims cannot be considered to be obvious over this combination of references. M.P.E.P. §2143.

The Examiner argues that the ability to provide improved absorption in the lower digestive tract is merely a statement of intended future use which carries no weight in determining patentability, and that any cilostazol composition is "able" to be released in the lower intestine insofar as it can be formulated into a colon-specific administration form.

However, an object of the present invention is to provide a cilostazol preparation for oral administration which is capable of releasing cilostazol at the lower portion of the digestive tract. This means that the cilostazol preparation according to the present invention after orally administering it, can be widely absorbed ranging from the stomach or small intestine to the large intestine at the lower portion of the digestive tract. See page 5, lines 1 to 16 of the specification.

In any event, because WO'382 does not teach any particle size for the cilostazol and Liversidge teaches only a particle size below that claimed, it is submitted the Examiner has not established a prima facie case of obviousness with this combination of references.

Its withdrawal as a ground of rejection and the allowance of the claims is therefore requested.

It is believed claims 32-50 are in condition for allowance.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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